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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,010	10/25/2001	Jonathan W. Nyce	EPI-00312	5176

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,010	NYCE, JONATHAN W.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *160-162,165 and 187-190* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *160-162,165 and 187-190* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.00

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 14, 2005 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed June 14, 2005, and amendment and response to the Final Office Action (mailed December 14, 2004), filed June 14, 2005 wherein claims 160-162, 165, 187-190 have been amended. Claims 1-159, 163-164, and 166-186 are cancelled previously.

Currently, claims 160-162, 165 and 187-190 are pending in this application.

Claims 160-162, 165 and 187-190 are examined on the merits herein.

As recorded in the Advisory Action April 25, 2005, Applicant's amendment filed September 9, 2004 that amends claim 160 has been considered and found persuasive to remove the rejection of Claims 160-162, 165 under 35 U.S.C. 112, first paragraph, as containing new matter of record in the previous Office Action December 14, 2004.

The terminal disclaimer filed March 14, 2004, disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of

U.S. 5,527,789 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Therefore, the obviousness-type double patenting rejection as being unpatentable over U.S. 5,527,789 of record in the Final Office Action December 14, 2004 is withdrawn.

Specification Objection

The instant specification is objected to under 37 CFR 1.77, as to the amended title filed March 14, 2005 wherein the instant specification has been amended as to title to read "Dehydroepiandrosterone Compositions and Formulations for Treating Respiratory Diseases".

The new title is deemed to insert **new matter** into the specification since the specification as originally filed does not provide support for "Treating Respiratory Diseases". The specification as originally filed describes that:

> "This invention concerns itself with a method of treating bronchoconstriction, lung inflammation and allergies, asthma, and cancer by administering an epiandrosterone, analogs thereof a ubiquinone, and/or their pharmaceutically acceptable salts. This invention also concerns itself with a method of treating adenosine depletion by administration of folinic acid or a pharmaceutically acceptable salt thereof." (see page 1, lines 11-17 of the specification herein).

Thus, one skilled in the art would clearly recognize that the scope of respiratory diseases, is different from bronchoconstriction, lung inflammation and allergies, asthma,

and cancer. Nowhere can the recitation "respiratory diseases" be found in the specification.

Therefore, the amended title fails to be accurate and descriptive of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 187-188 are rejected under 35 U.S.C. 102(b) as being anticipated by GB 2 240 472 (PTO-1449 submitted July 11, 2005).

GB 2 240 472 discloses a composition comprising dehydroepiandrosterones (DHEA) herein in a particle size less than 10 μm (see abstract, page 1; page 3 line 15; page 6 line 2-3). Thus, the particle size, less than 10 μm, reads on about 10 μm, as instantly claimed.

Thus, the disclosure of GB 2 240 472 anticipates claims 187-188.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 160-162, 165 and 187-189 are rejected under 35 U.S.C. 103(a) as being unpatentable over Prendergast (4,956,355 of record) in view of Lieberman et al. (Pharmaceutical Dosage Forms, page 110, of record) and "Remington: The Science and Practice of Pharmacy", 17th Ed, by Alfonso R Gennaro, 1985, page 1505 (PTO-892).

Prendergast discloses that particular dehydroepiandrosterones (DHEA) herein are useful in a pharmaceutical composition or a pharmaceutical formulation of enteral, parental, injectable, topical, inhalations or nasal inhalation administration (see col.5 lines 32-64, 49 and 63-64). See abstract, col.1 lines 36-57, col. 4-5 and claim 6. Prendergast also discloses the effective amounts of dehydroepiandrosterones in the composition and other agents and pharmaceutically acceptable excipients within the instant claim in the compositions therein (col.5).

Prendergast does not expressly disclose the particular ranges of particle size herein, about 1.0-5 μm or about 10-500 μm in size.

However, suitable particle sizes for inhalation are generally known and available to one of ordinary skill in the art. For example, "Remington: The Science and Practice of Pharmacy", 17th Ed, by Alfonso R Gennaro, 1985, teaches that the optimum particle size for preparation into the pulmonary cavity is of the order of ½ to 7 μm (see page 1505).

"Remington: The Science and Practice of Pharmacy", 20th Ed, by Alfonso R Gennaro, teaches that the optimum size for inhalations is known to be 0.5-0.7 μm into the pulmonary cavity (see page 735 the right column).

The book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6th Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column).

Lieberman et al. teaches that a skilled artisan in pharmaceutical science would clearly knowledge that the granulation, determination of size, or size reduction of a solid pharmaceutical formulation, e.g., in nasal inhalation formulation, have several benefits, for example, as taught in a text book "Pharmaceutical Dosage Forms" Tables, (Volume 2) Ed. by Herbert A. Lieberman, Leon Leachman, and Joseph B. Schwartz (1989) at page 110.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation, since particular dehydroepiandrosterones (DHEA) herein are known to be in a pharmaceutical composition for inhalations or nasal inhalation administration based on Prendergast.

As discussed above, the optimum size for inhalations is known to be 0.5-0.7 μm, ½ to 7 μm into the pulmonary cavity according to "Remington: The Science and Practice

of Pharmacy", and the fine particle size for inhalations is known to range 0.5-5 μm according to "Pharmaceutical Dosage Forms and Drug Delivery System". Thus, the dehydroepiandrosterones compositions of Prendergast for inhalations or nasal inhalation intrinsically comprise dehydroepiandrosterones particles having about 1-5 μm or about 10-500 μm in size.

Moreover, the known teachings of these books clearly support the examiner's position that it is obvious to one of ordinary skill in the art that using conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 160, 165 and 187-190 are rejected under 35 U.S.C. 103(a) as being unpatentable Nyce (5,527,789, of record) in view of Lieberman et al. (Pharmaceutical Dosage Forms, page 110) and "Remington: The Science and Practice of Pharmacy", 17th Ed, by Alfonso R Gennaro, 1985, page 1505 (PTO-892).

Nyce discloses a pharmaceutical composition comprising the instant DHEA having the chemical formula (I) in a therapeutically effective amounts and the instant ubiquinone having the chemical formula (II) with n being from 1 to 12, 1 to 10, 6 to 10, or 10, in the therapeutically effective amounts, and a pharmaceutical carrier or diluent (see abstract, claims 13-19). Nyce also discloses the particular effective amounts of DHEA, i.e., 1-3600 mg/kg, 5-1800 mg/kg, or 20-100 mg/kg (see col.6 lines 6-7); and the particular effective amounts of ubiquinone, i.e., 1-1200 mg/kg, 30-600 mg/kg, or 50-150 mg/kg (see col.5 lines 64-66), within the instant claimed range, about 0.1-49% or about 1-20% w/w, since converting the known actual amount by actual weight to weight percentage in a composition, w/w, is considered well within conventional skills in pharmaceutical science, involving merely routine skill in the art. The pharmaceutical composition of Nyce further comprises a preservative, an antioxidant, a flavoring agent (e.g., sugar, see col.7 line 10), a buffering agent, a dispersant, or a surfactant (see col.6 line 67 to col.8 line 1, and col.7 lines 33-38) an inert base, glycerol (glycerin, see col.7 line 11-12). Nyce also discloses the instant forms of the formulation, e.g., nasal spay (see col.7 line 17) oral, rectal, topical, transdermal, nasal, or parenteral including

injectable (see col.5 lines 37-41, col.6 lines 40-67), in a solution (an aqueous liquor), suspension.

The cited prior art does not expressly disclose the particular particles of the active agents having size herein, about 1-5 μm or about 10-500 μm in size.

However, suitable particle sizes for inhalation are generally known and available to one of ordinary skill in the art. For example, "Remington: The Science and Practice of Pharmacy", 17th Ed, by Alfonso R Gennaro, 1985, teaches that the optimum particle size for preparation into the pulmonary cavity is of the order of ½ to 7 μm (see page 1505).

"Remington: The Science and Practice of Pharmacy", 20th Ed, by Alfonso R Gennaro, teaches that the optimum size for inhalations is known to be 0.5-0.7 μm into the pulmonary cavity (see page 735 the right column).

The book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6th Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column).

Lieberman et al. teaches that a skilled artisan in pharmaceutical science would clearly knowledge that the granulation, determination of size, or size reduction of a solid pharmaceutical formulation, e.g., in nasal inhalation formulation, have several benefits, for example, as taught in a text book "Pharmaceutical Dosage Forms" Tables, (Volume 2) Ed. by Herbert A. Lieberman, Leon Leachman, and Joseph B. Schwartz (1989) at page 110.

Moreover, suitable particle sizes for inhalation are generally known and available to one of ordinary skill in the art. For example, "Remington: The Science and Practice of Pharmacy", 20th Ed, by Alfonso R Gennaro, teaches that the optimum size for inhalations is known to be 0.5-0.7 μm or ½ to 7 μm into the pulmonary cavity (see page 735 the right column). The book "Pharmaceutical Dosage Forms and Drug Delivery System" by Ansel et al. 6th Ed, page 454-455, teaches that the fine particle size for inhalations is known to range 0.5-5 μm (see page 455, the left column).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine and granulate the dehydroepiandrosterones particles in range of size herein for nasal inhalation, since the nasal formulation or composition comprising two instant active agents is known based on Nyce. According to conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

The known teachings of these books clearly support the examiner's position that it is obvious to one of ordinary skill in the art that using conventional techniques to make inhalable, respirable or nasal formulation of the known active agents are considered well within the skill of artisan in pharmaceutical science, involving merely routine skill in

the art, in addition to suitable particle sizes for nasal inhalation generally known and being available to one of ordinary skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant is further requested to note that it is well settled that "intended use" of a composition or product, will not further limit claims drawn to a composition or product. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

Response to Argument

Applicant's arguments filed June 14, 2005 with respect to the rejections made under 35 U.S.C. 103(a) of record in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art. These remarks are believed to be adequately addressed by the obvious rejections presented above.

Additionally, Applicant's declaration of Dr. Cynthia B. Robinson (not inventor), submitted March 14, 2005 under 37 CFR 1.132, has been fully considered but is unpersuasive to overcome the rejections under 35 U.S.C. 103(a), since, first, even though the cited patents are silent about the particle sizes, the same composition comprising the same compound for inhalations or nasal inhalation administration is

clearly taught; it is known that inhalations or nasal inhalation forms require the particle size, 0.5-0.7 μm or 0.5-5 μm or ½ to 7 μm as instantly claimed according to Reimgton's book or the book "Pharmaceutical Dosage Forms and Drug Delivery System". Thus, the particle size limitation would be inherently present in the inhalation or nasal inhalation compositions of the prior art .

Second, the declaration provides no side-by-side comparison with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art, i.e., comparing the particle size related to the testing results with the cited prior art.

Therefore, the declaration of Dr. Robinson is not persuasive to rebut the prima facie case herein.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
August 25, 2005